

**REMARKS**

The Examiner has rejected claims 1-10 for obviousness-type double patenting over commonly assigned U.S. Patent No. 7,070,768 in view of U.S. Patent No. 5,290,562. It is believed that the Examiner is incorrect in this rejection because the present application is directed to a method of preventing the graying of mammalian hair or converting gray hair to the original pigment color while '768 Patent is directed to a method of providing an artificial tan to the skin and protecting the skin from the effects of ultraviolet radiation. (The Examiner agrees that the present claims do not relate to "a method (for) providing artificial tan to the skin and protecting the skin from the effects of ultraviolet radiation ...").

However the Examiner argues that because '562 teaches that increasing or stimulating melanin synthesis improves the retardation of grey hair together with increasing the melanin pigment, a skilled artisan would have expected to inhibit or retard graying of hair or improve the pigmenting with the compound of '768 because of its melanin stimulating activity.

This argument fails because applicant has not posited that the mechanism of action for the use of the compounds claimed in his method of preventing graying or converting grey hair is melanin synthesis. Thus, one of ordinary skill in the art would not have motivation to combine the melanin mechanism disclosure of the '562 patent with the disclosure of the compounds of the '768 patent. It is this absence of motivation which defeats the Examiner's combination of the above prior art patents to reject the claims for double patenting.

Nevertheless, to promote the prosecution of this application, the applicant's attorney has submitted a Terminal Disclaimer at the invitation of the Examiner to overcome this rejection.

The Examiner has rejected claims 1-10 under 35 U.S.C. 112, first paragraph, because "the specification, while being enabling for converting gray hair to the original pigment in the hair follicle

of a subject being treated by the instant composition, does not reasonably provide enablement for preventing graying of hair.”

The applicant believes that this rejection is also incorrect. The Examiner’s argument is that “(g)ray hair is caused due to a number of reasons, such as predisposing genetic factors, exposure to UV radiation, natural aging process etc. Further, despite the fact the external or physical causes such UV radiation from sunlight do not always result in gray hair in each and every individual exposed to the radiation. Further, there is no specific time line or age at which graying can occur in different individuals.”

The Examiner appears to be arguing that the “graying”, that applicant’s claimed method of treatment is preventing, is graying resulting from UV radiation. However, this limitation is not found in the present specification. Applicant believes that graying, resulting from any of the conditions cited by the Examiner as responsible for graying, such as genetic factors, natural aging, as well as UV radiation, will be prevented by the practice of the claimed inventive method.

In further support of his argument that the present claims are properly rejected under 35 USC 112, second paragraph the Examiner has also criticized the working examples for failure to show that “greying” is prevented for more than 6 months from the date of treatment. This criticism is improper because the applicant has not taken the position that a single treatment will prevent graying. In fact, assuming the Examiner is correct in his argument that the prevention of graying has been shown for only 6 months, this example fully supports the claims for prevention of graying. And why can’t the method of the invention be repeated, as many times as necessary, to prevent graying?

Again, the applicant has amended the original claims to delete the aspect of “prevention of greying” from the preferred method of treating (The broad claim has been retained in new claim 11 nevertheless, in view of the above argument).

The Examiner has rejected claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over

U.S. 6,262,105 to Johnstone.

The Examiner argues that “Johnstone discloses a method for stimulating the growth of hair comprising administering a composition comprising a prostaglandin or its derivatives to the skin or scalp. Johnstone teaches that the compounds are effective in not only stimulating hair growth but also in increasing the pigmentation of the lashes, which is a result of the melanin production. The prostaglandin compounds of Johnstone are similar to the instant compounds except for the variable X of the instant claims. While instant claims require X=NR<sub>2</sub>, where R is a H or an alkyl having 1-6 carbon atoms, Johnstone teaches compounds with ester group on the same position as that of instant X.”

The difference between the prostaglandin compounds of Johnstone and the prostamide compounds utilized in the present method, which difference the Examiner acknowledges, is critical for finding that the present invention is not obvious to Johnstone. (Note, that the endogenous prostaglandins are terminated with a carboxylic acid group. It is well known that the esters of such endogenous prostaglandins quickly hydrolyze in-situ to yield the corresponding endogenous prostaglandin. Thus, as a drug, the endogenous prostaglandins and the esters thereof are equivalent. However, the amides not hydrolyze to the carboxylic acid in situ.)

The applicant hereby submits a paper co-authored by Woodward, one of the co-inventors of bimatoprost, which is the preferred prostamide for use in the practice of the present invention. (See U.S. Patents 5,352,708 and 6,403,649.) The paper is entitled “Bimatoprost and Prostaglandin F<sub>2α</sub> Selectively Stimulate Intracellular Calcium Signaling in Different Cat Iris Sphincter Cells”, Experimental Eye Research, 80(2005) 135-145.

The author shows that the substitution of an amide group for the carboxylic acid of a prostaglandin results in the compound not being a prostaglandin. That is, the prostamide interacts at a separate receptor which is not a prostaglandin receptor. Thus, the biology of prostaglandins and prostamides is different. Therefore, the Examiner’s argument that “it would have been obvious for

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one of an ordinary skill in the art at the time of the instant invention to employ a prostaglandin having an amide or an ester group at the variable X of instant compounds and still use it for converting grey hair to the original pigment in hair follicles or retard graying of hair because a skilled artisan would have understood at that the activity or the efficacy of prostaglandin compounds is due their core prostaglandin structure and that the ester or an amide substitution would have minimal effect on the final hair stimulating or pigment producing activity" is incorrect. As noted above, the ester will function as the corresponding prostaglandin, but, as demonstrated in the paper, the amide reacts with a different receptor. The seemingly small difference in the chemical structure of the prostamides of the present invention, and the prostaglandins of Johnstone results in a completely different biology. (And a biological process is what is being claimed in this patent application.)

Thus, it is believed that the claims, as presently amended, are in condition for allowance. The Examiner is asked to reconsider and withdraw his rejection and pass the claims to issue.

Respectfully submitted,



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